Changes in cocaine consumption are associated with fluctuations in self-reported impulsivity and gambling decision-making

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Abstract: Background. In cross-sectional studies, cocaine users generally display elevated levels of self-reported and cognitive impulsivity. To what extent these impairments are stable v. variable markers of cocaine use disorder, and, thus, are pre-existing or drug-induced, has not yet been systematically investigated. Method. We conducted a longitudinal study with cocaine users who changed or maintained their consumption intensity, measuring self-reported impulsivity with the Barratt Impulsiveness Scale (BIS-11), and cognitive impulsivity with the Rapid Visual Processing task (RVP), Iowa Gambling task (IGT), and Delay Discounting task (DD) at baseline and at 1-year follow-up. We assessed 48 psychostimulant-naive controls and 19 cocaine users with decreased, 19 users with increased, and 19 users with unchanged cocaine intake after 1 year as confirmed by hair analysis. Results. Results of linear multilevel modelling showed significant group × time interactions for the BIS-11 total score and the IGT total card ratio. Increasers showed a trend for elevated scores, whereas decreasers exhibited reduced self-reported impulsivity scores within 1 year. Surprisingly, increasers’ IGT performance was improved after 1 year, whereas decreasers’ performance deteriorated. By contrast, neither RVP response bias B⃗ nor DD total score showed substantial group × time interactions. Importantly, BIS-11 and DD revealed strong test–retest reliabilities. Conclusion. Self-reported impulsivity (BIS-11) and decision-making impulsivity (IGT) covary with changing cocaine use, whereas response bias and delay discounting remain largely unaffected. Thus, self-reported impulsivity and gambling decision-making were strongly state-dependent in a stimulant-using population and may be suitable to monitor treatment success, whereas delay of gratification was confirmed as a potential endophenotype of stimulant addiction.

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Changes in cocaine consumption are associated with fluctuations in self-reported impulsivity and gambling decision-making

Lea M. Hulka1*, Matthias Vonmoos1*, Katrin H. Preller1, Markus R. Baumgartner2, Erich Seifritz3,4, Alex Gamma5, Boris B. Quednow1,4

1Experimental and Clinical Pharmacopsychology, Department of Psychiatry, Psychotherapy, and Psychosomatics, Psychiatric Hospital, University of Zurich, Switzerland
2Center of Forensic Hairanalytics, Institute of Forensic Medicine, University of Zurich, Switzerland
3Director of the Department of Psychiatry, Psychotherapy, and Psychosomatics, Psychiatric Hospital, University of Zurich, Switzerland
4Neuroscience Center Zurich, University of Zurich and Swiss Federal Institute of Technology Zurich, Switzerland
5Division of ADHD Research, Department of Psychiatry, Psychotherapy, and Psychosomatics, Psychiatric Hospital, University of Zurich, Switzerland

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*L. M. Hulka and M. Vonmoos share first authorship and are both corresponding authors:

Lea M. Hulka, PhD
Experimental and Clinical Pharmacopsychology
Psychiatric Hospital of the University of Zurich
Lenggstrasse 31
CH-8032 Zurich, Switzerland
Tel.: 0041-44-205-5835
Fax: 0041-44-205-5802
E-Mail: lea.hulka@bli.uzh.ch

Matthias Vonmoos, PhD, MA
Experimental and Clinical Pharmacopsychology
Psychiatric Hospital of the University of Zurich
Lenggstrasse 31
CH-8032 Zurich, Switzerland
Tel.: 0041-44-384-2666
Fax: 0041-44-384-3396
E-Mail: matthias.vonmoos@bli.uzh.ch
Abstract

Background: In cross-sectional studies, cocaine users generally display elevated levels of self-reported and cognitive impulsivity. To what extent these impairments are stable vs. variable markers of cocaine use disorder, and, thus, are pre-existing or drug-induced, has not been systematically investigated yet.

Methods: We conducted a longitudinal study with cocaine users who changed or maintained their consumption intensity, measuring self-reported impulsivity with the Barratt Impulsiveness Scale (BIS-11), and cognitive impulsivity with the Rapid Visual Processing Task (RVP), Iowa Gambling Task (IGT), and Delay Discounting Task (DD) at baseline and at one-year follow-up. We assessed 48 psychostimulant-naïve controls and 19 cocaine users with decreased, 19 users with increased, and 19 users with unchanged cocaine intake after one year as confirmed by hair analysis.

Results: Results of linear multilevel modelling showed significant group*time interactions for the BIS-11 total score and the IGT total card ratio. Increasers showed a trend for elevated, whereas decreasers exhibited reduced self-reported impulsivity scores within one year. Surprisingly, increasers’ IGT performance was improved after one year, whereas decreasers’ performance deteriorated. By contrast, neither RVP response bias nor DD total score showed substantial group*time interactions. Importantly, BIS-11 and DD revealed strong test-retest reliabilities.

Conclusion: Self-reported impulsivity (BIS-11) and decision-making impulsivity (IGT) co-vary with changing cocaine use, whereas response bias and delay discounting remain largely unaffected. Thus, self-reported impulsivity and gambling decision-making were strongly state-dependent in a stimulant-using population and may be suitable to monitor treatment success, whereas delay of gratification was confirmed as a potential endophenotype of stimulant addiction.
Introduction

Cocaine addiction is a debilitating chronically relapsing disorder that is characterised by persistent and compulsive drug-seeking despite harmful consequences (APA 1994). Cocaine is the most commonly used stimulant drug in Europe and the United States (EMCDDA 2014; UNODC 2014) and current lifetime prevalence rates in the populations are estimated at 4.2% in Europe and 14.3% in the United States (EMCDDA 2014; NSDUH 2014). Despite the high addiction liability of cocaine (Nutt et al. 2007), only a relatively small fraction of users (5 to 6%) made the transition from controlled drug use to drug dependence within the first year of use, whereas 15 to 16% developed dependency in the long run (Wagner & Anthony 2002).

Converging evidence points to a complex interplay of inherited genetic predispositions and environmental, social, and neurobiological factors contributing to the vulnerability to develop an addiction (Kendler et al. 2007; Kreek et al. 2005). It has been postulated that chronic drug use is associated with neuroadaptations in fronto-limbic brain circuits mediating reward, motivation, and memory processes, presumably resulting in behavioural inflexibility such as disrupted self-control and compulsive drug use (Goldstein & Volkow 2011). However, the emerging concept of addiction endophenotypes also highlights the role of pre-existing psychological, cognitive, and neurobiological factors that may render an individual more susceptible to initiate drug use and develop an addiction (2013; Ersche et al. 2012; Mahoney & Olmstead 2013). Important and somewhat conceptually overlapping key factors implicated in the initiation and maintenance of drug use are maladaptive decision-making, increased impulsivity propensities, and implicit cognitive processes such as attentional bias and implicit memory associations (Field et al. 2008; Lucantonio et al. 2012; Marhe et al. 2013; Stevens et al. 2014; Wiers & Stacy 2006). Overall, drug users attribute excessive attention to drug-related stimuli, rate them more positively than non-users, and exhibit reduced inhibitory control and increased impulsivity, leading to harmful compulsive drug use despite the occurrence of negative consequences.

To what extent impaired decision-making and increased impulsivity are drug-induced, pre-existing vulnerability factors, or a combination of both is, however, not entirely clear so far.
Decision-making refers to the ability to select an optimal course of action from multiple options, requiring ongoing updating and integrating of the value of present and potential actions (Fellows 2004; Lucantonio et al. 2012). Prior studies have consistently shown that dependent cocaine users exhibit disadvantageous decision-making strategies in tasks such as the Iowa Gambling Task (IGT) and preferences for smaller immediate over larger but delayed rewards as measured with the Delay Discounting Task (DD)(Bechara et al. 2002; Hulka et al. 2014; Kjome et al. 2010; Verdejo-Garcia et al. 2007). Impulsivity, a multi-facetted concept, is generally defined as a predisposed tendency toward rapid and unplanned reaction patterns without much foresight regarding possible consequences (Moeller et al. 2001a). Impulsive tendencies or trait impulsivity is generally assessed with self-report questionnaires, such as the Barratt Impulsiveness Scale (BIS), which presumably focus on stable personality characteristics (Patton et al. 1995; Stevens et al. 2014). Although self-report measures can provide valuable information, they can be limited if the subject lacks insight or answers in a socially desirable manner (Moeller et al. 2001a). Therefore, using an experimental approach to complement self-report measures of impulsivity with behavioural performance measures is essential. Behavioural or neurocognitive impulsivity has been proposed to include the two main components of impulsive action representing motor impulsivity and impulsive choice reflecting more cognitive parts of impulsivity (Winstanley et al. 2010). Impulsive action is generally measured with tasks assessing the ability to inhibit motor responses (e.g., Stop-Signal, Stroop, Go/No-go, and sustained attention tasks such as the Rapid Visual Processing [RVP]), while impulsive choice is either assessed with tasks quantifying the ability to tolerate delay of gratification such as the DD or with tasks measuring responses to reward and loss contingencies such as assessed in the IGT (Stevens et al. 2014; Winstanley et al. 2010). It has been suggested that impulsive action might be more associated with the development of cocaine addiction, while impulsive choice may contribute specifically to relapse of cocaine use (Winstanley et al. 2010). However, this hypothesis has been recently challenged as we did not find elevated motor impulsivity in cocaine dependence (Vonmoos et al. 2013b), while especially DD – a prototype of impulsive choice – has been proposed as a critical risk factor for the development of drug addiction as well (MacKillop 2013).
Elevated trait impulsivity has consistently been reported for dependent and recreational stimulant users (Reske et al. 2011; Vonmoos et al. 2013b), whereas results on behavioural impulsivity are somewhat mixed: some studies found dependent (Ersche et al. 2010; Perry & Carroll 2008; Verdejo-Garcia et al. 2008) and recreational cocaine users (CU)(Colzato et al. 2007) to be impaired in Stop-Signal or Go/No-go tasks, whereas we recently concluded from data of a large sample of relatively pure CU that neither dependent nor recreational cocaine use was associated with impairment in the Stop-Signal task (Vonmoos et al. 2013b). However, the inconsistent results regarding performance in Stop-Signal tasks may be explained by different task designs and parameter calculation procedures as well as different exclusion criteria of polytoxic drug use and psychiatric comorbidities (Vonmoos et al. 2013b).

Importantly, impaired decision-making and social cognition in CU have been associated with worse self-reported real-life functioning (Cunha et al. 2011; Preller et al. 2014) and more frequent drug relapse and treatment attrition (Aharonovich et al. 2006; Bechara 2003; Verdejo-Garcia et al. 2014). Moreover, elevated levels of impulsivity have been associated with an increased risk to initiate and continue drug use and a greater likelihood of relapse (for review see Stevens et al. 2014). Considering the impact of impaired decision-making and elevated impulsivity on real-life functioning and treatment outcome, it is important to better understand if the different facets of impulsivity are stable antecedent vulnerability factors – predisposing individuals to develop and maintain cocaine addiction – or rather drug-induced consequences. Moreover, it is not clear whether these behavioural deviances are reversible when drug use is reduced or completely ceased. Recently, we reported that CU, who had substantially increased cocaine use over the course of one year, exhibited worse cognitive performance compared to baseline, whereas those who decreased or ceased their cocaine use showed substantially improved cognitive performance, suggesting that cognitive impairment is partially cocaine-induced but also reversible (Vonmoos et al. 2014).

The primary goal of the present investigation was thus to determine which specific decision-making and impulsivity components are stable (addiction endophenotypes) vs. variable (drug-induced) markers of cocaine use disorder over the time-course of one year. For this purpose, we conducted a longitudinal study assessing trait impulsivity with the BIS-11, impulsive action with the RVP response
bias B”, and impulsive choice with the main IGT and DD parameters, at baseline and after one year. CU of the Zurich Cocaine Cognition Study (ZuCo²St) were categorized as decreasers, increasers, or equal users after the one-year follow-up based on a toxicological quantification of cocaine levels in hair samples. With regard to the BIS-11 and DD, we expected that scores would remain stable over the two assessments because the BIS-11 is regarded as a trait measure and also discounting preferences appear to be relatively stable over time (for review see MacKillop 2013). For the RVP B’’ we expected stable results as none of the few existing previous studies with CU displayed a substantial cocaine-associated effect on this parameter (Ersche et al. 2011; Vonmoos et al. 2013b). By contrast, we expected that the IGT performance would improve with decreased cocaine use and worsen with increased cocaine use as prior studies reported dose-dependent relationships between cocaine use and IGT performance (Verdejo-Garcia et al. 2007).
Materials and Methods

Participants

The eligible baseline sample of the ZuCo²St comprised 234 participants (138 CU, 96 healthy psychostimulant-naive controls [HC])(Hulka et al. 2014; Preller et al. 2014; Vonmoos et al. 2013a). One-hundred-and-thirty-two subjects (79 CU [57.3% of baseline], 53 HC [55.2%]) participated in the 1-year-follow-up. Hereof, 57 CU and 48 matched HC could be included in the longitudinal analysis (for details see online Supplementary Methods S1).

At baseline, exclusion criteria for all participants were clinically significant somatic diseases, neurological disorders, head injuries, family history of schizophrenia, obsessive-compulsive disorder, or bipolar disorder, or any medication affecting the CNS. Further exclusion criteria for CU were opioid use, polytoxic drug use patterns, or DSM-IV axis I psychiatric disorders (except for cocaine, nicotine, and alcohol abuse/dependence, former affective disorders, and attention deficit hyperactivity disorder). At baseline, all CU met the following inclusion criteria: cocaine as primary drug of choice, cocaine use >0.5 g/month, and abstinence duration of <6 months. Exclusion criteria for HC were DSM-IV axis I psychiatric disorders (excluding nicotine dependence) and regular illegal drug use (>15 lifetime occasions, except occasional cannabis use).

Participants were asked to abstain from illegal substances for >72h and from alcohol for >24h. Compliance was controlled by urine screens (semi-quantitative enzyme multiplied immunoassay method) and 6-month hair toxicology (Vonmoos et al. 2013a). The study was approved by the Cantonal Ethics Committee of Zurich. All participants provided written informed-consent statements and were compensated for their participation.

Cocaine user groups

Cocaine user groups were determined based on a combination of absolute (±0.5 ng/mg cocaine)(Bush 2008; Cooper et al. 2012) and relative (>10% increase/decrease in the robust hair toxicology parameter cocaine_{total})(Hoelzle et al. 2008) changes in cocaine concentration in the hair samples between baseline and follow-up. CU who met both criteria were categorized as increasers or decreasers accordingly, whereas CU who met none or only one criterion were classified as equal users.
Accordingly, CU were divided into three equally sized groups: Whereas 19 CU with increased cocaine use and 19 CU with decreased cocaine use met the according change criteria, a third group of 19 CU displayed equal cocaine use and met neither the cut-off-criteria for increased nor decreased cocaine use (*increaser* mean±SD +30.4±61.9 ng/mg [+297%], range +0.5 to +268.5 ng/mg [+20% to +5374%]; *decreaser* -10.6±26.7 ng/mg [-72%], -116.9 to -0.6 ng/mg [-100% to -12%]; *equal user* -0.1±0.5 ng/mg [-2%], -1.9 to +0.5 ng/mg [-100% to +720%]).

**Procedure**

The test procedure was similar in both test sessions. The Structured Clinical Interview for DSM-IV axis I disorders (SCID-I; APA 1994) was carried out by trained psychologists. Drug use was assessed by means of a structured and standardized interview for psychotropic drug consumption (Quednow *et al.* 2004). For matching reasons, pre-morbid verbal intelligence was measured with a German version of a multiple choice vocabulary intelligence test (MWT-B; Lehrl 1999). Attention Deficit Hyperactivity Disorder (ADHD) symptoms were assessed with the ADHD Self-Rating Scale (ADHD-SR; Roesler *et al.* 2004), and symptoms of depression with the Beck Depression Inventory (BDI; Beck *et al.* 1961). Smoking severity was assessed with the Fagerström Test of Nicotine Dependence (FTND; Heatherton *et al.* 1991) and craving for cocaine with the Brief Cocaine Craving Questionnaire (CCQ; Sussner *et al.* 2006). Smoking intensity and cocaine craving were assessed to control for their potential acute effects on test performance (Franken 2003). Trait impulsivity was assessed with the BIS-11 (Patton *et al.* 1995). The two components of cognitive impulsivity *impulsive action* and *impulsive choice* were measured by means of the response bias $B'$ (an analogue to the response bias beta from the signal detection theory; Green & Swets 1966) drawn from the sustained attention task Rapid Visual Processing (RVP) of the Cambridge Automated Neuropsychological Test Battery (CANTAB; Elliott *et al.* 1996) as well as the discounting rate described by parameter $k$ from the DD Task (Kirby *et al.* 1999), and the IGT parameter total ratio (number of good cards-number of bad cards)(Bechara *et al.* 2002), respectively. At follow-up, a parallel test-version was used for the IGT. Detailed task descriptions for the RVP, IGT, and DD can be found in the online Supplementary Methods S2.
Statistical analysis

Statistical analyses regarding demographic data and drug use patterns (Table 1) as well as baseline test scores were performed with SPSS Statistics 19.0 (IBM, Switzerland). Frequency data were analyzed by means of Pearson’s chi-squared test and quantitative data by analyses of variance (ANOVA) or Student’s t-tests. All other analyses derived from the xtmixed command in Stata 12.1 for Macintosh (StataCorp. 2011). Regression modelling involved a series of linear multilevel models (also known as linear mixed, random-effects, or random-coefficient models)(Gelman & Hill 2007; Locascio & Atri 2011; Tabachnik & Fidell 2006).

All dependent variables were divided by their respective standard deviations to aid in model interpretation. Predictors evaluated were: group (increasers, decreasers, equal users, controls), time (dummy variable with levels baseline and follow-up), group*time interaction, female sex, age (in 10-year-steps), level of education (years), age of onset of cocaine use (in 5-year-steps), verbal IQ (in steps of 5), amount of Swiss Francs available in the last 12 months (ordinal variable with levels 0-15000, 15000-30000, 30000-60000, 60000-90000, 90000-120000, >120000), FTND score (divided by standard deviation), smoker (yes/no), ADHD-SR score (divided by standard deviation), adult ADHD (yes/no, DSM-IV criteria), BDI score (divided by standard deviation), BDI depression (yes/no, cut-off ≥18), CCQ score (divided by standard deviation), years of cocaine use, cumulative cocaine use in grams (transformed by natural logarithm because of violation of normality distribution), cocaine in hair samples (pg/mg), positive urine screen for cocaine (yes/no), and cocaine level in urine toxicology (ng/ml, log-transformed). Continuous predictors were centered on their grand means. In addition to some of the predictors (see above), the dependent variable DD-k total was log-transformed as well (further details of the statistical analysis are given in online Supplementary Methods S3).

Figure 1 shows the effects of group and time for the four main dependent variables, even if the main effects and/or interactions of group and time were not statistically significant in the final models that are reported in Table 2. In such cases, these effects were added to the final model and the figures were derived from these extended models.
Results

Demographic and clinical characteristics and drug use

The four groups did not significantly differ regarding age, sex distribution, verbal IQ, years of education, smoking status, and length of interval between the two study assessments (Table 1). Moreover, all three CU groups showed similar BDI (p_{Sidak, post-hoc}>.97) and ADHD-SR (p_{Sidak, post-hoc}>.99) sum scores, but exhibited distinctively higher values than HC (p_{BDI}=.08 to .006, p_{ADHD-SR}=.03 to .007).

At baseline, all three CU groups did not display significant differences in the self-reported cocaine use parameters and hair concentrations. However, the increaser and decreaser groups clearly featured a stronger current and cumulative cocaine use than the equal user group although the differences were not statistically significant. Furthermore and in accordance with the inclusion criteria, the data showed a clear domination of cocaine compared to other illegal drug use. At follow-up, increasers had a three- to four-fold higher cocaine concentration in the hair samples compared to the baseline value, whereas decreasers’ values dropped by about three quarters, while the equal users’ values remained relatively stable.

Impulsivity and decision-making scores

Barratt Impulsiveness Scale (BIS-11). At baseline, a combined CU group (including increasers, decreasers, and equal users) differed significantly from the HC group in the total score (T_{103}=2.98, p<.01) and all three subscales FI to FII (T_{103}=2.32 to 2.83, p=.02 to .006) as previously shown in Vonmoos et al. (2013b). The most striking finding was the significant group*time interaction (p<.01) in the BIS-11 total score with increasers showing a trend for elevated self-reported impulsivity over time (p=.12), whereas decreasers displayed significantly reduced self-reported impulsivity within one year (p<.05). Equal users’ (p=.86) and HC’s total scores remained comparatively stable (Figure 1A; a p-value for HC is not available because this group was dropped from the regression model due to collinearity). Table 2 shows that this pattern of significant group*time interactions (increaser vs. decreaser) can also be seen in the BIS-11 primary subscales FI (attentional impulsiveness, p<.05) and FII (motor impulsiveness, p<.01). Whereas none of the groups revealed significant time effects in attentional impulsiveness (p_{dec}=.17, p_{inc}=.08, p_{equal}=.28, p_{HC}=.48), decreasers showed a significant
reduction in the self-reported motor impulsiveness ($p_{dec}<.01, p_{inc}=.13, p_{equal}=.92, p_{HC}=.18$). For the BIS-11 subscale FIII (non-planning impulsiveness) no significant group*time interaction (increaser vs decreaser) was found ($p=.15$).

Additionally, BIS-11 total, attentional, and motor impulsiveness scores correlated strongly with ADHD-SR sum scores (all $p<.002$). Furthermore, BIS-11 total, attentional, and nonplanning scores were positively associated with BDI depression (all $p<.05$). BIS-11 total ($p<.05$) and nonplanning scores ($p<.001$) positively co-varied with craving scores, and a later age of cocaine onset was linked to reduced motor impulsiveness ($p<.01$). However, this latter effect was no longer significant when controls were excluded from the analysis.

*Rapid Visual Processing (RVP response bias $B''$).* For $B''$, no baseline differences between CU and HC occurred ($T_{103}=-1.04, p=.30$) (see also Vonmoos *et al.* 2013b) and in the longitudinal analysis there was no significant effect regarding group, time, or their interaction. The only significant finding was a weak positive association with duration of cocaine use ($p<.05$), which was no longer significant when excluding the control group from the analysis (Table 2, Figure 1B).

*Delay discounting (DD $k$ total).* At baseline, CU and HC strongly differed regarding $k$ total ($T_{103}=-3.40, p<.001$), as shown before (Hulka *et al.* 2014). Longitudinally, $k$ total showed no statistically significant group and/or time effects. However, a 100% increase in the cumulative lifetime dose of cocaine was associated with roughly a 20% decline in scores of the ability to delay gratification – i.e. to forego immediate smaller in favour of delayed larger rewards. Moreover, a 100% raise in the FTND score was associated with a 30% decrease in scores for delayed gratification (Table 2, Figure 1C).

*Iowa Gambling Task (IGT total ratio).* Baseline scores of the IGT total ratio did not differ between CU and HC ($T_{102}=.72, p=.47$). In the longitudinal analysis, a significant group*time interaction was found for the IGT total ratio ($p<.05$, Table 2, Figure 1D, for a detailed distribution of IGT scores for each group at t1 and t2 see online Supplementary Figure S1). Without any
statistically significant main effect of group, *decreasers’* scores fell during the 1-year-interval ($p=.11$), whereas those of the *increasers* improved ($p=.09$). Concretely, this means that *decreasers* chose significantly fewer favourable cards at follow-up. *Equal users’* ($p=.34$) and HC’ ($p=.54$) total ratio scores remained fairly stable. Age ($p<.01$), an ADHD diagnosis ($p<.10$), and a positive smoking status ($p<.01$) were related to decreases in IGT performance of roughly 1/3 SD.

*Test-retest reliability.* In three of the four main variables, HC displayed slightly higher test-retest reliability scores than the combined CU group (Table 3) but the differences were not significant ($z<.80$, $p>.20$). Moreover, the BIS-11 total score showed a remarkable strong test-retest reliability, whereas the response bias B’’ featured the smallest but nonetheless significant test-retest reliability in HC and CU.
Discussion

The present longitudinal study investigated to what extent impaired decision-making and elevated impulsivity levels in CU may represent stable and pre-existing addiction endophenotypes vs. variable state markers depending on the quantity of cocaine used. The most striking finding was that self-reported levels of impulsivity strongly co-varied with changing cocaine use patterns. Accordingly, CU who substantially decreased their cocaine intake within one year reported significantly lower levels of impulsive behaviour, whereas CU who increased their consumption reported by trend higher levels of subjectively perceived impulsivity. By contrast, cognitive impulsivity measures capturing impulsive action (response bias $B''$) and impulsive choice (delay discounting) did not significantly differ with increasing or decreasing cocaine use over the course of one year. Contrary to our expectations, CU who decreased their cocaine intake during the one-year-interval chose fewer favourable cards in the IGT at the second study assessment, whereas CU who increased their consumption showed a slightly improved performance. Nonetheless, there seemed to be a linkage between worse decision-making at baseline and a subsequently increased cocaine use pattern suggesting that impaired decision-making might indeed be a risk factor for increasing cocaine use.

The results of the present study are somewhat surprising and call some existing assumptions into question. The BIS has been regarded to reflect a relatively stable trait component of subjectively experienced impulsivity levels (Stevens et al. 2014). However, our results revealed that CU who increased their consumption over the time-course of one year perceived themselves by trend as more impulsive, whereas CU who decreased their use rated themselves as less impulsive. Although the BIS reliably differentiated CU form HC, and thus might overall reflect a trait component, it is not as stable in drug using populations as previously assumed. Therefore, the BIS may be useful to assess how subjectively perceived levels of impulsiveness in CU co-vary with drug consumption. Moreover, Littlefield et al. (2009) have also provided evidence that impulsivity measures assessed in questionnaires change over time. Previously, we have already shown that BIS ratings were elevated in dependent CU using substantially higher amounts of cocaine than in recreational CU with a much less pronounced cocaine use pattern (Vonmoos et al. 2013b). It is noteworthy that differences ($\Delta_{t2-t1}$) in self-reported impulsivity between the two testing sessions did not significantly correlate with changes
in cognitive impulsivity tasks (CU: $r < .30, p > .05$; HC: $r < - .30, p > .05$; total sample: $r < -.15, p > .25$). This finding is in line with prior studies conducted in our lab where trait impulsivity was only weakly correlated with behavioural impulsivity task measures (Hulka et al. 2014; Quednow et al. 2007; Vonmoos et al. 2013b) and, thus, underlines the multi-facetted concept of the impulsivity construct. The reasons why users, who changed their cocaine use pattern, perceived their impulsivity levels to be more or less pronounced, remains to be determined in further investigations. One could speculate though that the subjective recognition of changes in impulsivity is more sensitive than the behavioural measures or that specific facets of impulsivity were not covered by our behavioural tasks. Alternatively, CU’ personal thoughts, attitudes, and intentions to change their cocaine use might have influenced subjectively reported impulsivity levels. Accordingly, *increasers* may be more concerned with their loss of control over drug intake and/or may also experience more aversive consequences due to their increased cocaine use fostering worries. *Decreasers* on the other hand may have perceived themselves as less impulsive because they had a desire to reduce their cocaine use and made a conscious effort to control their impulsivity. Correspondingly, research on attentional bias modification and substance use has shown that individuals who express a desire to reduce their use respond much better to treatment and show less impulsivity (Wiers & Stacy 2006). Moreover, it has been shown that increased impulsivity in the BIS is associated with more treatment dropouts and shorter treatment duration in CU (Moeller et al. 2001b; Patkar et al. 2004). Therefore, treatment approaches should foster awareness in CU that they often act impulsively and without foresight for negative consequences, but that these cognitive-behavioural tendencies can be reduced with mindfulness-based and other cognitive-behavioural relapse prevention strategies (Dakwar & Levin 2013).

It is also noteworthy that self-reported attentional and motor impulsivity were significantly associated with more pronounced ADHD symptoms. These results are in line with findings from our cross-sectional study (Vonmoos et al. 2013b) as well as with previous studies postulating a substantial comorbidity of ADHD with substance use disorders (van Emmerik-van Oortmerssen et al. 2012). Unfortunately, we omitted to assess the ADHD-SR questionnaire at the follow-up test session and are
therefore not able to directly analyse the co-variation of changes in ADHD symptoms with changes of impulsivity measures.

In the present study, temporal discounting preferences as measured by DD did not vary with increased or decreased cocaine use, which is in line with previous propositions that intertemporal discounting preferences reflect a stable aspect of personality and can be considered as a trait marker (Odum 2011a, b). A growing body of evidence corroborates our finding by showing that individual discounting preferences in adolescents and adults are relatively stable over numerous time intervals ranging from one week to multiple years (for review see MacKillop 2013). In addition, more pronounced delay discounting preferences have been suggested to be predictive of the initiation and escalation of drug use (2013; Ersche et al. 2012; Mahoney & Olmstead 2013) as well as poor treatment responses in human CU (Washio et al. 2011). Furthermore, a prospective study yielded evidence that stronger tendencies to prefer immediate smaller over larger but later available amounts are associated with negative outcomes in the financial, academic, and health domains (Mischel et al. 2011). Altogether, the results of the present study and prior findings suggest that more pronounced delay discounting rates may be regarded as a relatively stable addiction endophenotype increasing the risk to initiate and maintain drug use (MacKillop 2013; Odum 2011a, b).

Impulsive action measured by the RVP response bias B’’ was not significantly shifted in our CU and did not co-vary with changing drug use patterns. These findings are consistent with the previously published results from the cross-sectional part of the ZuCo2St showing that neither recreational nor dependent CU differed from controls regarding RVP B’’ and Stop-Signal task performance (Vonmoos et al. 2013b). Accordingly, the ecological validity of the RVP response bias B” regarding the measurement of addiction-related impulsive action might be questioned.

The finding that CU who decreased their consumption chose fewer favourable cards in the IGT at the second assessment is somewhat puzzling. In the cross-sectional analysis published previously (Hulka et al. 2014), we found that although dependent CU performed slightly worse than HC, the effect was not as pronounced as shown in previous studies (Bechara et al. 2002; Kjome et al. 2010; Verdejo-Garcia et al. 2007). We speculated that these differences might be explained by the fact that we paid our participants with real money according to their performance, which is in contrast to most
prior studies reporting substantial differences between CU and HC. In line with our hypothesis are the results obtained in another study conducted by Vadhan et al. (2009) where CU were paid in real money and also did not perform significantly worse than HC in the IGT, suggesting that motivational factors may influence IGT performance in drug users. It is further noteworthy that while cocaine use patterns did not significantly differ between the user groups at baseline, decreasers had a higher cumulative cocaine usage than equal users and increasers. Therefore, we cannot fully rule out that decreasers were overall more impaired in their IGT performance due to their more pronounced cocaine use, which may not have been detected in the baseline assessment because of low statistical power.

There are some limitations inherent to this study: First, the sample sizes are relatively small for multilevel analyses. However, the data were also analysed with mixed design analyses of covariance yielding comparable results (not reported here). Second, in addition to the increased cocaine consumption, increasers also drank more alcohol than decreasers and tested positive for recent cocaine use more frequently than decreasers. However, the rise in weekly alcohol use was based on an increased alcohol intake in only three of 19 cocaine increasers and excluding these subjects did not alter the main results. Third, although the group assignment of increasers, decreasers, and equal users was based on objective hair toxicology capturing the past six months, for the first six months of the time interval we had to rely on self-reported drug measures. Fourth, although our sample consisted of CU with relatively little polytoxic drug use, it should be mentioned that at baseline, cocaine increasers used low but significantly higher amounts of MDMA (0.04 vs. 0.01 tablet per week) and used amphetamine (3.3 vs. 1.3 years) for a longer period than decreasers. Furthermore, at follow-up cocaine increasers revealed a slightly higher use of MDMA and methylphenidate compared to baseline and had an additional augmentation in weekly alcohol use. Whereas the change in MDMA use was less than half a tablet per week, the difference in methylphenidate consumption was explained by a single individual. However, exclusion of the single methylphenidate user did not change the main results in separate analyses. Thus, although changes in other drugs should be considered as a contributing factor to our results, it seems reasonable that compared to the strong increase in cocaine use, the effect of changed use of other drugs is likely rather small. Fifth, our CU groups differed from
controls regarding ADHD and depressive symptoms, which is in accordance with the current literature (Swendsen & Merikangas 2000; Wilson 2007). However, we tried to overcome this constraint by introducing these variables in the multilevel regression analyses.

These one-year longitudinal data indicate for the first time that self-reported impulsivity and impulsive choice requiring the integration of risk, reward, and loss contingencies (as measured with the IGT) co-vary with changing cocaine use, while a response bias measure and delay discounting preferences remain largely unaffected. Accordingly, self-reported impulsivity and gambling decision-making measures are less suitable for predicting the risk to develop a cocaine use disorder but might be used to monitor treatment success. By contrast, the preference for immediate smaller rewards over larger delayed rewards seems to be a stable trait marker for cocaine use and, thus, may represent a suitable endophenotype for stimulant addiction.
Author contributions
LMH and MV obtained the data, wrote the manuscripts, were partly involved in data analysis. KHP was involved in data collection and revised the manuscript. MRB conducted and interpreted the hair analyses. AG was responsible for the multilevel data analysis and revised the first draft of the manuscript. ES gave financial support and revised the manuscript. BBQ designed the study, wrote and revised the manuscript, and bears responsibility for data acquisition and analyses.

Funding and Disclosure
The authors declare no conflict of interest. The study was supported by grants from the Swiss National Science Foundation (SNSF; grant No. PP00P1-123516/1 and PP00P1-146326/1) and the Olga Mayenfisch Foundation.

Acknowledgements
We are grateful to Daniela Jenni, Kathrin Küpeli, and Franziska Minder for excellent support of recruitment and assessment of the participants.
References


**Figure legend**

**Figure 1.** Predicted values for baseline (t1) and follow-up (t2) are shown. (A) Development of BIS-11 total scores within one year. Control group data in raw values (predicted data are not available because this group was dropped from the regression model due to collinearity). Group*time interaction (increaser*decreaser) p<.01. * p<.05 time effect for cocaine *decreasers*. (B) Development of RVP response bias B’’ within one year. (C) Development of delay discounting parameter k within one year. Control group data in raw values (predicted data are not available because this group was dropped from the regression model due to collinearity). (D) Development of the IGT total ratio within one year. Group*time interaction (increaser*decreaser) p<.05.
### Table 1. Demographic data and pattern of drug use.

<table>
<thead>
<tr>
<th></th>
<th>Controls (n=48)</th>
<th>Cocaine Increaser (n=19)</th>
<th>Cocaine Decreaser (n=19)</th>
<th>Equal cocaine users (n=19)</th>
<th>F/χ²</th>
<th>df</th>
<th>dferr</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Weeks between t1 and t2</strong></td>
<td>58.2 (10.1)</td>
<td>59.3 (12.1)</td>
<td>61.9 (14.5)</td>
<td>64.8 (16.3)</td>
<td>1.37*</td>
<td>3,101</td>
<td>.26</td>
<td></td>
</tr>
<tr>
<td><strong>Age, y</strong></td>
<td>30.3 (8.9)</td>
<td>31.5 (9.4)</td>
<td>31.4 (8.3)</td>
<td>27.0 (5.6)</td>
<td>1.20*</td>
<td>3,101</td>
<td>.31</td>
<td></td>
</tr>
<tr>
<td><strong>Sex (f/m)</strong></td>
<td>16/32</td>
<td>3/16</td>
<td>5/14</td>
<td>8/11</td>
<td>3.49b</td>
<td>3</td>
<td>.32</td>
<td></td>
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<tr>
<td><strong>Verbal IQ (MWL-B)</strong></td>
<td>107.6 (10.0)</td>
<td>102.9 (9.7)</td>
<td>103.8 (7.1)</td>
<td>104.5 (9.1)</td>
<td>1.57*</td>
<td>3,101</td>
<td>.20</td>
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<td><strong>Education, y</strong></td>
<td>10.8 (1.8)</td>
<td>10.4 (1.8)</td>
<td>10.0 (1.5)</td>
<td>10.3 (1.6)</td>
<td>0.96a</td>
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<td></td>
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<td><strong>ADHD-SR score (0-22)</strong></td>
<td>7.7 (5.2)</td>
<td>13.5 (9.4)*</td>
<td>14.1 (6.8)*</td>
<td>14.4 (10.2)**</td>
<td>6.31a</td>
<td>3,101</td>
<td>.001</td>
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<tr>
<td><strong>ADHD DSM IV (y/n)</strong></td>
<td>0/48</td>
<td>4/15</td>
<td>3/16</td>
<td>4/15</td>
<td>10.72b</td>
<td>3</td>
<td>.01</td>
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<tr>
<td><strong>BDI score (0-63)</strong></td>
<td>3.5 (3.3)</td>
<td>7.3 (8.0)</td>
<td>8.7 (6.5)**</td>
<td>8.1 (6.2)*</td>
<td>5.83a</td>
<td>3,101</td>
<td>.001</td>
<td></td>
</tr>
<tr>
<td><strong>BDI depression (y/n)</strong></td>
<td>0/48</td>
<td>1/18</td>
<td>1/18</td>
<td>2/17</td>
<td>4.46b</td>
<td>3</td>
<td>.22</td>
<td></td>
</tr>
</tbody>
</table>

#### Cocaine

- **Times per week**
  - 1.6 (1.8)  1.0 (1.3)  0.6 (0.6)  2.51c  2.54  .09
- 1.1 (0.8)  0.3 (0.3)***  0.3 (0.2)***  15.57d  2.54  <.001

- **Grams per week**
  - 8.2 (23.3)  11.4 (23.9)  2.5 (7.6)  0.98c  2.54  .38
- 31.7 (56.5)  3.1 (5.9)*  2.6 (7.9)  4.81f  2.54  .01

- **Max. dose (grams/day)**
  - 6.8 (4.4)  5.9 (6.4)  3 (3.1)  1.78c  2.54  .18
- 3.7 (2.5)  3.1 (2.8)  1.7 (1.5)*  3.53c  2.54  .04

- **Cumulative dose**
  - 1188 (1635)  3698 (8585)  394 (563)  2.21c  2.54  .12
- 91 (119)  49 (89)  18 (25)*  3.35c  2.54  .04

- **Last consumption (days)**
  - 18.5 (25.1)  20.8 (22.2)  42.2 (49.7)  2.72c  2.54  .08
- 7.0 (6.3)  81.4 (145.1)  58.2 (116.6)  2.38c  2.54  .10

- **Cocaine craving (0-7)**
  - 19.8 (9.5)  17.7 (7.2)  18.4 (7.7)  0.35c  2.54  .71
- 20.5 (10.8)  15.8 (6.2)  15.1 (7.7)  2.32c  2.54  .11

- **Current cocaine dependence (n/y)**
  - 11/8  13/6  18/1  7.06c  2   0.03

- **Hair analysis (ng/mg)**
  - 10.3 (29.2)  14.9 (32.2)  3.2 (9.9)  0.99c  2.54  .38
- 40.7 (76.1)  4.2 (8.2)*  3.2 (9.4)*  4.38e  2.54  .02

- **Cocaine**
  - 8.2 (23.3)  11.4 (23.9)  2.5 (7.6)  0.98c  2.54  .38
- 31.7 (56.5)  3.1 (5.9)*  2.6 (7.9)  4.81f  2.54  .01

- **Benzoylecgonine**
  - 1.9 (5.5)  3.1 (7.6)  0.6 (1.9)  0.99c  2.54  .38
- 8.3 (19.6)  1.0 (2.2)  0.4 (1.2)  2.82d  2.54  .07

- **Cocaineethylene**
  - 1.0 (2.8)  0.9 (2.8)  0.3 (0.8)  0.45c  2.54  .64
- 1.2 (2.1)  0.3 (1.0)  0.7 (2.1)  1.02c  2.54  .37

- **N-ac-nor-cocaine**
  - 0.2 (0.5)  0.4 (0.8)  0.1 (0.3)  1.11c  2.54  .34
- 0.6 (1.4)  0.1 (0.1)  0.1 (0.3)  2.81c  2.54  .07

- **Urine toxicology (n/p)**
  - 48/0  14/5  16/3  18/1  3.17b  2   0.21
- 7/12  18/1  16/3  17.90b  2   <.001

### Alcohol

- **Grams per week**
  - 119.9 (136.8)  169.4 (129.2)  155.3 (146.4)  132.3 (86.4)  0.81a  3,101  .49
- 104.3 (88.6)  259.7 (244.5)***  127.4 (141.4)*  146.7 (95.1)  5.74a  3,101  .001

- **Years of use**
  - 13.3 (8.8)  13.7 (7.6)  12.0 (7.3)  9.9 (5.0)  1.04a  3,101  .38
- 14.0 (8.7)  14.8 (7.5)  12.6 (7.9)  11.1 (5.5)  0.89a  3,101  .45

### Nicotine

- **Smoking (y/n)**
  - 37/11  14/5  14/5  14/5  0.16b  3   .98
- 40/8  15/4  13/6  15/4  1.83b  3   .61

- **Cigarettes per day**
  - 8.7 (8.7)  12.8 (11.2)  9.5 (8.2)  12.2 (8.3)  1.32a  3,101  .27
- 8.2 (8.7)  13.4 (12.0)  8.2 (7.8)  12.7 (8.9)  2.23a  3,101  .09

- **Years of use**
  - 9.3 (8.3)  10.4 (8.9)  12.7 (10.3)  9.2 (6.3)  0.78a  3,100  .51
- 10.5 (8.8)  12.5 (8.6)  12.6 (9.9)  9.5 (6.7)  0.66a  3,101  .58

- **FTND score**
  - 1.8 (2.2)  3.4 (2.7)  2.8 (2.7)  2.2 (2.1)  2.45a  3,101  .07
- 1.6 (2.3)  3.9 (3.0)**  2.7 (3.0)  2.6 (2.2)  3.73a  3,101  .01
### Cannabis

**Grams per week**

<table>
<thead>
<tr>
<th></th>
<th>0.6 (1.6)</th>
<th>3.3 (8.9)</th>
<th>1.2 (2.3)</th>
<th>1.2 (2.6)</th>
<th>1.81</th>
<th>0.5 (1.6)</th>
<th>2.1 (4.6)</th>
<th>1.1 (2.7)</th>
<th>0.9 (1.6)</th>
<th>1.74</th>
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<tbody>
<tr>
<td>Years of use</td>
<td>4.5 (4.9)</td>
<td>9.5 (8.5)</td>
<td>10.1 (9.7)</td>
<td>7.8 (5.9)</td>
<td>4.26</td>
<td>4.6 (5.9)</td>
<td>10.5 (9.8)</td>
<td>8.6 (9.7)</td>
<td>8.4 (6.2)</td>
<td>3.54</td>
</tr>
<tr>
<td>Cumulative dose (grams)</td>
<td>980 (3985)</td>
<td>3199 (5899)</td>
<td>2606 (6359)</td>
<td>19323 (4309)</td>
<td>1.13</td>
<td>53.4 (180)</td>
<td>217.8 (526.5)</td>
<td>84.7 (189.6)</td>
<td>55.0 (94.7)</td>
<td>1.83</td>
</tr>
<tr>
<td>Last consumption (days)</td>
<td>39.3 (55); n=22</td>
<td>10.0 (10); n=14</td>
<td>25.4 (33); n=12</td>
<td>28.7 (41); n=15</td>
<td>1.46</td>
<td>36.5 (78); n=22</td>
<td>9.7 (25); n=13</td>
<td>8.6 (9.7)</td>
<td>8.4 (6.2)</td>
<td>1.83</td>
</tr>
<tr>
<td>Urine toxicology (n/p)</td>
<td>42/6</td>
<td>15/4</td>
<td>14/5</td>
<td>12/3</td>
<td>2.08</td>
<td>0.0 (0.0)</td>
<td>0.1 (0.2)**</td>
<td>0.0 (0.0)</td>
<td>0.1 (0.2)**</td>
<td>53.4 (180)</td>
</tr>
</tbody>
</table>

### Amphetamine

**Grams per week**

<table>
<thead>
<tr>
<th></th>
<th>0.0 (0.1)</th>
<th>0.1 (0.1)*</th>
<th>0.0 (0.1)</th>
<th>0.0 (0.1)</th>
<th>3.17</th>
<th>0.0 (0.0)</th>
<th>0.1 (0.2)**</th>
<th>0.0 (0.0)</th>
<th>0.1 (0.2)**</th>
<th>19.19</th>
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<tbody>
<tr>
<td>Years of use</td>
<td>0.0 (0.0)</td>
<td>3.3 (4.0)**</td>
<td>1.3 (3.1)</td>
<td>1.4 (3.0)</td>
<td>8.45</td>
<td>0.1 (0.5)</td>
<td>3.2 (4.9)**</td>
<td>2.7 (5.5)*</td>
<td>1.9 (3.5)</td>
<td>5.07</td>
</tr>
<tr>
<td>Cumulative dose (grams)</td>
<td>0.0 (0.1)</td>
<td>56.0 (177.6)*</td>
<td>16.2 (35.9)</td>
<td>2.8 (5.8)</td>
<td>2.58</td>
<td>0.0 (0.1)</td>
<td>4.4 (8.9)**</td>
<td>1.4 (3.5)</td>
<td>1.9 (6.0)</td>
<td>5.07</td>
</tr>
<tr>
<td>Last consumption (days)</td>
<td>121.6 (-); n=1</td>
<td>73.6 (62); n=10</td>
<td>90.9 (81); n=3</td>
<td>61.8 (60); n=7</td>
<td>0.34</td>
<td>17.5 (-); n=1</td>
<td>35.7 (32); n=8</td>
<td>99.8 (108); n=4</td>
<td>65.9 (23); n=3</td>
<td>1.84</td>
</tr>
<tr>
<td>Hair analysis (ng/mg)</td>
<td>0.0 (0.0)</td>
<td>0.1 (0.2)*</td>
<td>0.0 (0.0)</td>
<td>0.0 (0.0)</td>
<td>3.43</td>
<td>0.0 (0.0)</td>
<td>0.1 (0.2)</td>
<td>0.1 (0.2)</td>
<td>0.0 (0.0)</td>
<td>2.56</td>
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</tbody>
</table>

### MDMA

**Tablets per week**

<table>
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<th></th>
<th>0.0 (0.0)</th>
<th>0.1 (0.1)**</th>
<th>0.0 (0.0)</th>
<th>0.0 (0.0)</th>
<th>5.11</th>
<th>0.0 (0.0)</th>
<th>0.4 (0.9)**</th>
<th>0.0 (0.0)*</th>
<th>0.1 (0.1)</th>
<th>4.49</th>
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</thead>
<tbody>
<tr>
<td>Years of use</td>
<td>0.3 (1.0)</td>
<td>3.5 (4.5)**</td>
<td>2.4 (4.6)</td>
<td>2.1 (3.8)</td>
<td>5.35</td>
<td>0.2 (1.4)</td>
<td>3.8 (5.5)**</td>
<td>3.2 (5.6)*</td>
<td>2.6 (4.3)</td>
<td>5.26</td>
</tr>
<tr>
<td>Cumulative dose (tablets)</td>
<td>1.3 (4.0)</td>
<td>108.8 (249.7)**</td>
<td>18.7 (46.2)</td>
<td>14.6 (39.9)</td>
<td>4.61</td>
<td>0.2 (0.8)</td>
<td>17.0 (49.3)*</td>
<td>2.8 (5.2)</td>
<td>4.3 (7.1)</td>
<td>2.91</td>
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<td>Last consumption (days)</td>
<td>5.0 (-); n=1</td>
<td>89.9 (65); n=7</td>
<td>40.2 (34); n=4</td>
<td>56.4 (43); n=6</td>
<td>1.32</td>
<td>91.2 (30); n=3</td>
<td>41.6 (55); n=6</td>
<td>47.8 (48); n=5</td>
<td>69.7 (36.4); n=8</td>
<td>1.10</td>
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<tr>
<td>Hair analysis (ng/mg)</td>
<td>0.0 (0.0)</td>
<td>0.3 (0.7)</td>
<td>0.4 (1.5)</td>
<td>0.2 (0.5)</td>
<td>1.69</td>
<td>0.0 (0.0)</td>
<td>0.5 (0.8)**</td>
<td>0.1 (0.3)</td>
<td>0.2 (0.4)</td>
<td>5.71</td>
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### GHB

**Cumulative dose (pipettes)**

<table>
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<th>0.5 (0.7)</th>
<th>0.5 (1.7)</th>
<th>4.5 (17.8)</th>
<th>1.71</th>
<th>0.0 (0.0)</th>
<th>0.0 (0.0)</th>
<th>0.0 (0.0)</th>
<th>1.2 (5.2)</th>
<th>1.68</th>
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</table>

### Hallucinogens

**Cumulative dose (times)**

<table>
<thead>
<tr>
<th></th>
<th>0.9 (2.2)</th>
<th>27.9 (72.8)*</th>
<th>9.9 (22.9)</th>
<th>6.3 (14.3)</th>
<th>3.10</th>
<th>0.0 (0.0)</th>
<th>1.1 (1.6)***</th>
<th>0.6 (1.5)</th>
<th>0.4 (0.8)</th>
<th>6.18</th>
</tr>
</thead>
</table>

### Methylyphenidate

**Cumulative dose (tablets)**

<table>
<thead>
<tr>
<th></th>
<th>0.0 (0.0)</th>
<th>20.2 (60.4)</th>
<th>0.5 (2.3)</th>
<th>41.3 (144.6)</th>
<th>2.05</th>
<th>0.0 (0.1)</th>
<th>67.7 (239.5)</th>
<th>0.3 (0.6)</th>
<th>1.5 (4.6)</th>
<th>2.80</th>
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<tr>
<td>Hair analysis (ng/mg)</td>
<td>0.0 (0.0)</td>
<td>0.0 (0.1)</td>
<td>0.0 (0.0)</td>
<td>0.0 (0.0)</td>
<td>1.40</td>
<td>0.0 (0.0)</td>
<td>0.1 (0.2)*</td>
<td>0.0 (0.0)</td>
<td>0.0 (0.0)</td>
<td>2.99</td>
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</tbody>
</table>

Means and standard deviations. Significant p values are shown in bold.

1. ANOVA (all groups, with significant Sidak post-hoc test vs. control group: *p<.05; **p<.01; ***p<.001; vs. cocaine increaser: °p<.05). 2. χ²-test (all groups/cocaine users only) for frequency data. 3. ANOVA (cocaine users only, with significant Sidak post-hoc test vs. cocaine increaser: °p<.05; °°°p<.001). 4. Average use during the last 6 months. 5. Craving for cocaine was assessed by the CCQ. 6. Last consumption is averaged only for persons who used the drug in the last 6 months. 7. Urine toxicology (neg/pos) are based on cut-off value for Cocaine = 150 ng/ml and for Tetrahydrocannabinol 50 ng/ml (Substance Abuse and Mental Health Services Administration 2008). The χ²-test for cocaine includes only cocaine users, the χ²-test for cannabis includes all groups. 8. Hair samples were voluntary and data are missing for three controls. 9. Parameters at follow-up refer to the 1-year period between t1 and t2. 10. SCID-I diagnosis according to DSM-IV criteria (APA, 1994).
**Table 2. Coefficients (standard errors) of final multilevel regression models with standardized dependent variables**

<table>
<thead>
<tr>
<th></th>
<th>RVP</th>
<th>BIS-11</th>
<th>BIS-11 FI</th>
<th>BIS-11 FII</th>
<th>BIS-11 FIII</th>
<th>DD</th>
<th>IGT</th>
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<tr>
<td></td>
<td>Response bias B^{-a}</td>
<td>Total score{a}</td>
<td>Attentional imp.{a}</td>
<td>Motor imp.{a}</td>
<td>Nonplanning imp.{a}</td>
<td>K total [log]{a}</td>
<td>Total score{a}</td>
</tr>
<tr>
<td><strong>Time</strong></td>
<td></td>
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<tr>
<td>t</td>
<td>0.234 (0.15)</td>
<td>0.303+ (0.17)</td>
<td>0.273 (0.18)</td>
<td></td>
<td></td>
<td>0.403+ (0.24)</td>
<td></td>
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<tr>
<td><strong>Group</strong></td>
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</tr>
<tr>
<td>Equal users (vs inc{c})</td>
<td>0.144 (0.28)</td>
<td>0.175 (0.22)</td>
<td>0.208 (0.29)</td>
<td></td>
<td></td>
<td>-0.232 (0.31)</td>
<td></td>
</tr>
<tr>
<td>Decreasers (vs inc{c})</td>
<td>0.294 (0.28)</td>
<td>0.074 (0.22)</td>
<td>0.403 (0.29)</td>
<td></td>
<td></td>
<td>-0.077 (0.31)</td>
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<tr>
<td>Controls (vs inc{c})</td>
<td></td>
<td>0.198 (0.19)</td>
<td>0.135 (0.25)</td>
<td></td>
<td></td>
<td>-0.174 (0.26)</td>
<td></td>
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<tr>
<td><strong>Group x time</strong></td>
<td></td>
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<tr>
<td>Equal users (vs inc{c})</td>
<td>-0.206 (0.22)</td>
<td>-0.489* (0.24)</td>
<td>-0.292 (0.26)</td>
<td></td>
<td></td>
<td>-0.173 (0.34)</td>
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<tr>
<td>Dec (vs inc{c})</td>
<td>-0.568** (0.21)</td>
<td>-0.532* (0.24)</td>
<td>-0.836** (0.25)</td>
<td></td>
<td></td>
<td>-0.786* (0.34)</td>
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</tr>
<tr>
<td>Controls (vs inc{c})</td>
<td></td>
<td>-0.229 (0.20)</td>
<td>-0.423* (0.21)</td>
<td></td>
<td></td>
<td>-0.313 (0.28)</td>
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<tr>
<td><strong>Demographics</strong></td>
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<tr>
<td>Age [per 10 y]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-0.310** (0.09)</td>
<td></td>
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<tr>
<td><strong>Clinical status{c}</strong></td>
<td></td>
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<tr>
<td>ADHD-SR score</td>
<td>0.385*** (0.10)</td>
<td>0.669*** (0.06)</td>
<td>0.260** (0.09)</td>
<td></td>
<td></td>
<td>-0.516+ (0.27)</td>
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<tr>
<td>ADHD DSM IV [y/n]</td>
<td>0.130* (0.06)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.149 (0.07)</td>
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<tr>
<td>BDI score</td>
<td></td>
<td>0.595* (0.26)</td>
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<tr>
<td>BDI depression [y/n]</td>
<td></td>
<td></td>
<td>0.149 (0.07)</td>
<td></td>
<td></td>
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<tr>
<td>Smoking FTND score</td>
<td></td>
<td></td>
<td></td>
<td>0.310* (0.13)</td>
<td></td>
<td>-0.215** (0.08)</td>
<td></td>
</tr>
<tr>
<td>Smoking [y/n]</td>
<td></td>
<td></td>
<td>-0.282+ (0.15)</td>
<td></td>
<td></td>
<td>-0.348 (0.18)</td>
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</tr>
<tr>
<td><strong>Cocaine use related{c}</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Age of onset [per 5 y]</td>
<td>-0.161+ (0.09)</td>
<td>-0.075+ (0.04)</td>
<td>-0.147** (0.05) d</td>
<td>-0.178+ (0.10)</td>
<td></td>
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<tr>
<td>Craving score [per SD]</td>
<td>0.190* (0.07)</td>
<td></td>
<td></td>
<td>0.237*** (0.07)</td>
<td></td>
<td>-0.275+ (0.16)</td>
<td></td>
</tr>
<tr>
<td>Years of use [years]</td>
<td>0.035* (0.02) d</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Cumulative dose [grams; log]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.177* (0.08)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Significance levels: +p<.10; *p<.05; **p<.01; ***p<.001.

* All dependent variables divided by standard deviation.  

{a} Increasers.  

{b} No longer significant when excluding controls.  

{c} Only trend-level significant when excluding controls.  

{d} Values at baseline (t1).

The table shows all coefficients that are relevant for the final models. Principally, final models included only predictors at p<.10. However, in case of any significant interaction effects (group*time), the table additionally displays the single terms (group, time).
Table 3. One-year test-retest reliability between baseline and one-year follow up in controls and cocaine users

<table>
<thead>
<tr>
<th></th>
<th>Controls (n=48)</th>
<th>Cocaine users (n=57)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BIS total score</td>
<td>.81***</td>
<td>.75***</td>
</tr>
<tr>
<td>RVP response bias B'</td>
<td>.30*</td>
<td>.35**</td>
</tr>
<tr>
<td>DD k total [log]</td>
<td>.52***</td>
<td>.43***</td>
</tr>
<tr>
<td>IGT total score</td>
<td>.45**</td>
<td>.43**</td>
</tr>
</tbody>
</table>

Pearson’s product-moment correlation.
Significance levels: *p<.05; **p<.01; ***p<.001.
Fig. 1B

- -- equal users  -- decreasers  -- increasers  -- controls

Response Bias B''

.9

.95

.95

.9

t1

t2
Online Supplementary Material

Changes in cocaine consumption are associated with fluctuations in self-reported impulsivity and gambling decision-making

Lea M. Hulka1*, Matthias Vonmoos1*, Katrin H. Preller1, Markus R. Baumgartner2, Erich Seifritz3,4, Alex Gamma5, Boris B. Quednow1,4

1Experimental and Clinical Pharmacopsychology, Department of Psychiatry, Psychotherapy, and Psychosomatics, Psychiatric Hospital, University of Zurich, Switzerland
2Center of Forensic Hairanalytics, Institute of Forensic Medicine, University of Zurich, Switzerland
3Director of the Department of Psychiatry, Psychotherapy, and Psychosomatics, Psychiatric Hospital, University of Zurich, Switzerland
4Neuroscience Center Zurich, University of Zurich and Swiss Federal Institute of Technology Zurich, Switzerland
5Division of ADHD Research, Department of Psychiatry, Psychotherapy, and Psychosomatics, Psychiatric Hospital, University of Zurich, Switzerland

*L. M. Hulka and M. Vonmoos share first authorship and are both corresponding authors:
Lea M. Hulka, PhD     Matthias Vonmoos, PhD, MA
Experimental and Clinical Pharmacopsychology     Experimental and Clinical Pharmacopsychology
Psychiatric Hospital of the University of Zurich     Psychiatric Hospital of the University of Zurich
Lenggstrasse 31     Lenggstrasse 31
CH-8032 Zurich, Switzerland     CH-8032 Zurich, Switzerland
Tel.: 0041-44-205-5835     Tel.: 0041-44-384-2666
Fax: 0041-44-205-5802     Fax: 0041-44-384-3396
E-Mail: lea.hulka@bli.uzh.ch     E-Mail: matthias.vonmoos@bli.uzh.ch
Methods S1

Participant recruitment: Participants were recruited in the greater area of Zurich from January 2010 until March 2013. Study participants were recruited via advertisements in local newspapers, online media, drug prevention and treatment centers, psychiatric hospitals, and by word of mouth. Eight-hundred-and-four prospective participants underwent a standardized telephone interview, whereof 240 subjects were tested in the cross-sectional study. Six participants were not re-invited to participate in the follow-up study (refusal of study participation, psychiatric disorders or first-grade family member with schizophrenia). The remaining 234 participants (138 cocaine users, 96 healthy psychostimulant-naive controls [HC]) (Hulka et al. 2014; Preller et al. 2014; Vonmoos et al. 2014) were contacted and invited for a follow-up test session twelve months after baseline testing. One-hundred-and-two participants (59 cocaine users, 43 controls) were not available for the follow-up study due to different reasons (no response, losing interest, time reasons, death). One-hundred-and-thirty-two participants (79 CU [57.3% of baseline], 53 HC [55.2%]) participated in the 1-year-follow-up. Twenty-seven of these subjects (22 cocaine users, 5 controls) had to be excluded from the final analyses due to hair analyses revealing illegal drug use not allowed by our exclusion criteria (e.g., opioids or excessive MDMA intake) or due to starting use of psychotropic medication (e.g., antipsychotics or antidepressants), leaving a final sample of 57 CU and 48 matched HC.
Methods S2

**Rapid Visual Processing Task (RVP):** The RVP is a visual continuous performance task from the Cambridge Neuropsychological Test Automated Battery (CANTAB; www.cantab.com) using predefined sequences of three digits presented at a rate of 100 per minute to assess sustained attention over a period of 4 min. In order to assess impulsive action, we assessed the response bias B” reflecting the tendency to respond regardless of the presence of a target and can therefore be interpreted as a measure for impulsive behavior (Nuechterlein et al. 2008).

**Iowa Gambling Task (IGT):** The IGT assesses the ability to choose between favorable card decks yielding lower gains but also a lower risk for losses eventually resulting in long-term benefit and unfavorable card decks resulting in higher gains but also higher losses leading to long-term loss. A computerized version of Grasman and Wagenmakers (University of Amsterdam, Netherlands) was used (http://purl.oclc.org/NET/rgrasman/jscript/IowaGamblingTask). Participants had to draw 100 cards from four different card decks, each containing 50 cards. The net score of good and bad cards drawn served as the dependent variable. At the end of the task, points were converted by the factor .002 and paid out in real money. All participants started out with 4000 points, with the maximum number of points that could be gained at 8000, equaling 16 CHF.

**Delay Discounting (DD):** In the DD, 27 choices between immediately available lower monetary rewards and higher rewards available with a temporal delay were presented. The discounting rate, how strongly larger but later available rewards are discounted, was calculated with the Formula $V=A/(1+kD)$ ($V$ is the present value of the delayed reward $A$ at delay $D$, and $k$ is a free parameter that determines the discount rate) (Mazur 1987). A computerized version (implemented in Presentation®) of the DD paradigm according to Kirby et al. (1999) was used. The steepness of discounting of delayed rewards (expressed as $k$ total; the larger the parameter $k$, the stronger the discounting of larger delayed rewards) was used as the dependent variable.
Methods S3

Linear multilevel models: For any given dependent variable, to assess whether a random intercept was appropriate, we fitted a model without predictors and checked whether a) the standard deviation of the random intercept was significantly different from zero and b) whether the Intraclass Correlation Coefficient (ICC), which is the proportion of between-subjects variance, was significantly greater than zero. This was the case for all models. The appropriateness of a random slope was assessed for each level-1 predictor of each model separately, using one-tailed Likelihood-Ratio-Tests. In one case, a random slope was added. Finally, model fit, in particular linearity of the relation between outcome and predictors, was checked by residual vs fitted plots.

Because the number of parameters in multilevel models should be adjusted to the sample size (Tabachnik & Fidell 2006), we reduced the number of predictors using a strategy adopted from (Hosmer & Lemeshow 2000): to fit univariate models, predictors at p<.2 were included in a full model. Predictors at p>.1 were then eliminated step-by-step, starting with the least statistically significant one. It was ensured that when eliminating a predictor, coefficient estimates for the remaining predictors did not change by more than about 25%. Final models included only predictors at p<.10.

In predictors relevant only to CU such as level or duration of consumption, collinearity was to be expected with the grouping variable, since the HC always have zero-values, while CU have positive values. Therefore, all models were repeated in a dataset excluding HC to check for coefficient differences in cocaine-related predictors. In a few cases these coefficients were no longer statistically significant.
Figure S1: Distribution of IGT total ratio scores for each group at t1 and t2.

Figure S1
References


